Longevity technology

Royal jelly is published as making mice live 25 (27%) longer, and queen bees live about 36 months, 12 to 24 times longer than other bees; noting that insect chemicals can cause mammals to live longer, it is possible other long lived insects could have chemicals that cause greater longevity. The mice that were longevized with royal jelly were fed it orally, bringing up the possibility of change to the proteins in it; some insects, queen termites, live 50 years, with some possibility of 100 years, feeding ground up insects to mice, both orally and as enteric capsule or coated material could find out if the ground up material of long lived insects cause greater longevity; another approach is to extract circulatory fluid (hemolymph) from

these insects and find out if it makes yeast or c elegans or fish live longer, notably, fish as vertebrates could be notably suggestive of mammalian activity; another insect to screen for longevity chemicals are cicada nymphs (17 years), beetles of the genus Eleodes (up to 17 years)

longevity technology: I perceive I read playing back EEGs causes the brain to be better at learning and can reactivate emotions; it is possible that rather than EEG, electrical recordings from the surfaces of children and 16 year olds could be played back at the body surface to find out if it has any longevizing, wellness, or healthspan effects; this could be tested on nude mice, and might go well with the body and tissue thickness of mice as proof of concept; at humans something like a wireless recharging near body

surface implant (kind of like a pacemaker) could provide the youthful EEG-like stimulus, notably it is possible that wave and frequency variants like nodal, antinodal or possibly depth-reaching electrical solitons https://phys.org/news/2006-05-solitons-electronics.html (dissipative solitons, 100 times farther travel than regular solitons) could be used; notably, some current levels and alternate voltages for the EEG-like frequencies could be used to possibly reach tissues at greater depth, as could wrist-to-wrist or leg to wrist, or even head to calf electrode placement

EEG playback technology: playing back EEGs to cause beneficial cognitive effects using different voltages or currents to reach deeper into tissue, notably though some currents and voltages might verge

into tDCS (although AC-like) which is a different thing; the previously described gelatin capsule sized piezoelectric frond hair adhering and head skin seeking technology could also do some tDCS as well as EEG recording, playback and software based synthesis; children's EEGs could also be played back at adults to find out if there were child-mind effects as well as, just possibly, longevising, wellness, or healthspan effects (seems unlikely, but is possible), notably children have more delta waves, and these occur during sleep, although less so at older people, these child EEG frequencies could be played back while adults sleep; this could be tested on rats, or some larger animal like cows, sheep, or horses

Longevity technology: Some biologically occuring tings do

rapamycin like things https://www.ncbi.nlm.nih.gov/pubmed/29165314 It is possible that mutating these plants, then screening their chemicals on yeast and things like c elegans with 96 well plate technology could create much larger rapamycin like longevity chemicals at plants, these could then be genetically engineered into delicious as well as ubiquitous plant foods to create longevity producing fruits, grains, and food products like pasta, pizza, potato products, breading, there is also the possibility that moving these gnes and gene products from plants to eggs and milk could be beneficial

a molecular variant or rapamycin, rapamycin preassociated (attached) to a protein makes it 2000 times more active, “To probe the affinities involved in the formation of the

FKBP.rapamycin.FRB complex, we used fluorescence polarization, surface plasmon resonance, and NMR spectroscopy. Analysis of the data shows that rapamycin binds to FRB with moderate affinity (K(d) = 26 +/- 0.8 microM). The FKBP12.rapamycin complex, however, binds to FRB 2000-fold more tightly (K(d) = 12 +/- 0.8 nM) than rapamycin alone. No interaction between FKBP and FRB was detected in the absence of rapamycin. These studies suggest that rapamycin's ability to bind to FRB, and by extension to mTOR, in the absence of FKBP is of little consequence under physiological conditions.” It is possible some molecular version of rapamycin (a rapalog) could cause mTOR activity without FKBP protein, FKBP has immunoeffects so that molecule could have less immunoeffects than rapamycin

Rapamycin that is more water soluble, “clinical development of its formulations was hampered due to its poor solubility and undesirable distribution in vivo. Chemical modification of rapamycin presents an opportunity for overcoming the obstacles and improving its therapeutic index. The objective of this study is to develop a drug-polymer conjugate to increase the solubility and cellular uptake of rapamycin.

METHODS:

We developed the rapamycin-polymer conjugate using a novel, linear, poly(ethylene glycol) (PEG) based multiblock copolymer. Cytotoxicity and cellular uptake of the rapamycin-polymer conjugate were evaluated in various cancer cells.

RESULTS:

The rapamycin-polymer conjugate provides enhanced solubility in water compared with free rapamycin and shows profound activity against a panel of human cancer cell lines. The rapamycin-polymer conjugate also presents high drug loading capacity (wt% ~ 26%) when GlyGlyGly is used as a linker. Cellular uptake of the conjugate was confirmed by confocal microscopic examination of PC-3 cells that were cultured in the presence of FITC-labled polymer (FITC-polymer).

CONCLUSION:

This study suggests that the rapamycin-polymer conjugate is a novel anti-cancer agent that may provide an attractive strategy for treatment of a wide variety of tumors.” hydrophilic rapamycin

combined with regular rapamycin could reach a wider variety of tissue types, combined they could cause greater than the 60% longevity increase published at mice

Optically activated rapamycin, “We developed an optically activated rapamycin dimer” perhaps a topical benefit

focusing rapamycin effect on just one tissue (kidney), “Thus subcapsular delivery of rapamycin-loaded microspheres successfully inhibited local fibrotic response in UUO with less systemic effects. Therapeutic effect of released rapamycin was most prominent in close vicinity to the implanted microspheres.”

longevity technology: Liver function genes, like SNPs, could be a source of new longevity drugs, gene therapy or

also germline gene modification, “To identify the pathways that could be responsible for rapamycin's longevity effect, we analyzed the transcriptome of liver from 25-month-old male and female mice fed rapamycin starting at 4 months of age. Few changes (<300 transcripts) were observed in transcriptome of rapamycin-fed males; however, a large number of transcripts (>4,500) changed significantly in females. Using multidimensional scaling and heatmap analyses, the male mice fed rapamycin were found to segregate into two groups: one group that is almost identical to control males (Rapa-1) and a second group (Rapa-2) that shows a change in gene expression (>4,000 transcripts) with more than 60% of the genes shared with female mice fed Rapa. Using ingenuity pathway analysis, 13

pathways were significantly altered in both Rapa-2 males and rapamycin-fed females with mitochondrial function as the most significantly changed pathway. Our findings show that rapamycin has a major effect on the transcriptome and point to several pathways that would likely impact the longevity.” They could do this analysis at a variety of tissues, including the gut, which I perceive I read secretes and might process a lot of physiochemicals

liposomes http://www.ijper.org/sites/default/files/IJPER_45_4_13.pdf

liposomes might or might not benefit rapamycin, a way to tell is if rapamycin has nootropic characteristics, possibly at a higher sample dose, and then see if a liposomal version causes more

nootropic effect, notably though liposomes might cause longer plasma half life and could possibly have different peak plasma concentrations so that might effect a nootropic effect

about 76% of some actual rapamycin liposomes get turned into liposomes, with the rest at the remaining fluid, that suggests drinking the extra fluid, or eating the trehalose it might be dried out on could provide another simultaneous, possibly different tissue specific activity of rapamycin

depending on if phosphatidylcholine or phosphatidyl serine turns into, or is highly similar to phosphatidic acid liposomes made of these might be nonpreferred, suggesting a different liposomal production method “the efficacy of rapamycin is dependent on the level of phosphatidic acid (PA), which is required for the assembly of

both mTORC1 and mTORC2 complexes. Rapamycin interacts with mTOR in a manner that is competitive with PA. Therefore, elevated levels of PA, which is common in cancer cells, increases the level of rapamycin needed to suppress both mTORC1 and mTORC2.”

liposome preservatives and how long liposomes last with refrigeration, “The use of cryoprotectants such as dextrose, sucrose, and trehalose may increase stability from hydrolysis. Also, samples may experience oxidation upon storage. The addition of small amounts of antioxidants during processing may stabilize the suspension and limit oxidation of the product. SUV should be stored above their transition temperature for no longer than ~24 hours. LUV may be store for a longer period of time if

stored at 4-8°C when not in use. Hydrolysis of the lipid begins to occur immediately resulting in monoacyl derivatives (Lyso lipids) which act as detergents and disrupt the membrane, thus permeabilizing the membrane. After ~5-7 days at 4-8°C the internal contents will begin to leak indicating hydrolytic degradation of the lipid. If membrane structure is not a critical parameter in your experiments, vesicles may be stored for 1-2 months with minimal (<10%) hydrolytic degradation.”

distilled water is likely a way to make liposomes be longer lasting, “or by binding metal ions that initially induced aggregation. However, the presence of aggregation can accelerate the process of coalescence of liposomes”

ions at a solution could cause

liposomes to last less long, that suggests when making liposomes drug and lecithin, or purified phosphatidylcholine, amounts at something like ultrasonication to make the most liposomes per volume, it is also possible filtering or centrifuging (?) liposomes could divide it from a fluid which might have uncombined, particularly oxidizable drug or phosphatidyl choline molecules

If there are longer versions of phosphatidylcholine they might make more durable liposomes, “Permeability and stability of liposomes are influenced by the rigidity/stiffness of the lipid bilayer.”

liposome size depends on how they are made, ultrasonication produced liposomes make “small unilamellar vesicles (SUV), 25 to 100 nm in size that consists of a single lipid bilayer.”

shaking a liposome making solution with your arms makes “Large unilamellar vesicles (LUV), 100 to 400 nm in size that consists of a single lipid bilayer. Multilamellar vesicles (MLV), 200 nm to several microns that consist of two or more concentric bilayers.” it is possible a combination of all three types reaches a wider variety of tissues and likely has greater physiological activity and physiological availability than rapamycin at an enteric capsule

“liposomes prepared by using combinations of some lipids follows the order of physical stability form the correlation of the mean volume diameter, zeta potential and pH , egg lecithin (PC)/cholesterol (CH)/stearylamine (SA) < PC/CH/phosphatidylserine (PS) < bovine brain ceramides

(CM)/CH/palmitic acid (PA)/CS < PC/CH/cholesteryl sulphate (CS) at 4°C, as well as at 25°C, 2122after a 6-month storage period" also, "Vesicles composed of saturated phospholipids were found more stable compared to phosphatidyl-choline(PC) liposomes"

Ethanol makes for better drug loading, "that rely on incubation temperatures above the phase transition temperature (Tc) of the bulk phospholipid to promote drug loading. In the absence of cholesterol, liposome permeability is enhanced at these temperatures which, in turn, can result in the collapse of the pH gradient and/or unstable loading. Doxorubicin loading studies, for example, indicate that the drug could not be loaded efficiently into cholesterol-free DSPC liposomes. this problem could be circumvented by the

addition of ethanol as a permeabilityenhancer.Doxorubicinload ingratesincholesterol-free DSPC liposomes were 6.6-fold higher in the presence of ethanol. In addition, greater than 90% of the added doxorubicin was encapsulated within 2 h at 37 °C, an efficiency that was 2.3-fold greater than that observed in the absence of ethanol.” also, “Optimal ethanol concentrations ranged from 10% to 15% (v/v) and these concentrations did not significantly affect liposome size, retention.”

Dissolve in etoh first, then put the water in perhaps, perhaps some solvent that rapamycin is more soluble in than water could be put in the ultrasonic liposome maker at a 1 part per 100 amount to heighten colubility, another way is to see if the pile of rapamycin dissolves whn you

stir the liposome making fluid

Liposomes can be dried over sorbitol, “formulation of proliposomes lipid dried over a fine particulate, water soluble support like sodium chloride, sorbitol or polysaccharides imparts adequate physical and chemical stability and are ideally suitable for lipophilic drugs” That might be functional with trehalose as well to absorb nonreacted fluids, while the trehalose might also preserve the liposomes

Trehalose as a liposome preservative, at lyophilized of liposomes, “aggregation of liposomes could be prevented by the formation of stable boundaries between the vesicles. The ability of cryoprotectants to form these stable boundaries has been attributed to their ability to replace the bound water around the bilayer

via interaction with the polar region of the lipid 36head group (water replacement hypothesis).” also, as to things like trehalose, “high concentrations (up to 30 mol.% in some cases) are required” (to where it is gooey)

the trehalose, possibly, could be added to the fluid ahead of ultrasonication, “In the preferred embodiment, the liposomes are made in the presence of the combination of at least one sugar (sucrose, trehalose, lactose, maltose and glucose)”

liposomes could increase plasma half life of rapamycin availability

antioxidants as liposome preservatives, “use of antioxidants like α-tochopherols, betahydroxy toluene (BHT)”

Rapamycin is made from fungi,

“Rapamycin and its analogs are clinically important macrolide compounds produced by Streptomyces hygroscopicus” so depending on how much rapamycin the fungi make those genes could be transferred to plants or perhaps mammals like humans

Rapamycin might last awhile at the body, there are three plasma half lifes I have read, .9 hours, 9 hours, and 56 hours, one thing online says, “The long elimination half-life of sirolimus necessitates a loading dose but allows once daily administration, which is more convenient”

Longevity technology: “Centenarians delay age-related methylation changes, and they can pass this methylation preservation ability on to their offspring.” suggests that drugs, or possibly some non-CRISPR CRISPR

like thing could duplicate longevity methylation at everybody

a-tocopherol looks kind of like phenylethylamine, perhaps putting a nitrogen on it, and maybe trimming away a couple CH3s that are on the long alkane distal to the cylic (bicyclic) part, as well as putting a halogen atom on it (I do not know if 2 grams, at numerous doses of a-tocopherol is beneficial or nonbeneficial) so that just a few milligrams or even micrograms rather than 350 mg is a fun dose, also halogenation might outcompete a-tocopherol at some valuable body location, it could be a thing though, a stimulant that is perhaps slightly beneficial

IGF1 (Insulin like growth factor) as well as insulin if modified, perhaps with gene therapy or germline genetic modification could produce IGF1 as

well as insulin that do sugar response things while being neutral to longevity, perhaps causing less AMPK activation (If that is what they do)

fetal environment as well as parental epigenetics are published as effecting longevity, methylation, ethylation and other epigenetic things could be modified with supplements or drugs during pregnancy to align the person the fetus becomes with highest longevity, wellness, and healthspan; I do not know if more methylation during pregnancy is the thing, or if just specif areas of DNA methylation are the thing, different tissues, at the devloping fetus have different epigentics,

How much food the parents eat makes a difference in progeny wellness, “There is consistent evidence from both mice and rat models that

modulating the maternal dietary status such as protein restriction during pregnancy can significantly affect lifespan", "F1 male mice exposed to maternal undernutrition during prenatal life produced F2 male offspring with impaired glucose tolerance and increased adiposity", Also, at humans, "F2-generation offspring of women who were exposed to the famine of 1944–1945 in the Netherlands (i.e., Dutch Hunger Winter) throughout the gestational period had 1.8 times more health problems in their adulthood than descendants of non-exposed women [70]. The offspring of the fathers, but not the mothers who suffered from intrauterine undernutrition during the Dutch famine also had a significantly greater weight and body mass index in their adult life than the descendants of parents unexposed to the famine", I

perceive this suggests that at the fetus different amounts of something like methylation (also acetylation, phosphorylation, methylation, phosphorylation, sumoylation, and ubiquitination) could effect longevity, which suggests drug localization of methyl donors could be beneficial, perhaps optimal methylation of the CNS and heart could be a longevity area, “the epigenetic code changes dramatically during the embryonic development of the organism to initiate differential gene expression patterns between various developing tissues. This code consists of chemical modifications of DNA and histone proteins that play a crucial role in packing the DNA by forming nucleosomes.” Acetylation promotes gene expression, perhaps rather than methylation acetylation of longevity genes could cause greater longevity,

also, “The dynamic “writing” and “erasing” of histone modifications are conducted by specific enzymes” suggesting that drugs that cause more beneficial enzymes to be produced, gene therapy as well as germline modification, particularly with tissue localization of beneficial amounts of enzymes could be beneficial, this could be a longevity techology; what one paper describes as socioeconomic adversity “In sons and grandsons of men born outside wedlock, a 1.64- and 1.83-fold excess risk of circulatory disease” Homesis also has an effect, so a drug or supplement that cause the right amount of stress, without the parents feeling the stress could be beneficial, “there is also evidence that exposure to mild stressors in early development can result in beneficial (hormetic) effects and that adaptive modulation

of epigenetic processes could significantly contribute to these effects [92–94]. There is also evidence that adaptive/hormetic effects can persist over several generations”, as a longveity wellness drug, it is possible that parents could make their epigenetics (methylation, acetylation phosphorylation, others) like those of persons at the 99.999the percentile of longevity,

marmosets, a primate, could be used to measure the effect of epigenetics on longevity

finding longevity genes other than those that effect mTOR and AMPK: they could look at all the rodents (mice, beavers), and all the bats, and find the ones with the least and most favorable mTOR and AMPK genetics,

then they could find the longest living rodents and bats with the least beneficial mTOR and AMPK genetics, it is possible that noting 33 year rodent lifespan difference the long lived non beneficial mTOR and AMPK rodents can be compared with the lifespan of rodents with highly favorable mTOR and AMPK genetics but lifespans of 1/2 to 1/4 or even 1/11 of that, then they can find the genes that cause the greater longevity even though mTOR and AMPK are least beneficial at the much longer lived rodents, also, they can just compare mice genetically modified to have highly beneficial mTOR and AMPK with the genes of beavers to find the beaver non-mTOR and non-AMPK genes that cause the greater longevity even though the beavers might have median mTOR and AMPK genetics; they can do the same thing with bats; The longevity

drug benefit is that on finding the longevity genes of rodents that outlive rodents with optimal mTOR and AMPK genetics 4 to 11 times then the products of those genes, and the actual genes, can then be placed at mice to find out if they are longevity drugs and genes, characterizing humans as to the amount of the new longevity genes activity and the amounts of their gene products, is also beneficial.

crispr rodent gene swap, find the longevity gene swapping beaver and mouse genes with CRISPR/cas9 to find out which non mTOR and AMPK genes cause mice to live much longer like the 35 year beavers

Longevity technology: